

**WE CLAIM:**

1. A microsphere comprising hyaluronan functionalized with a crosslinker at glucuronic acid sites of the hyaluronan, wherein the derivitized hyaluronan is crosslinked intramolecularly and intermolecularly.
2. The microsphere of claim 1, wherein the crosslinker is a dihydrazide having the formula:
$$\text{H}_2\text{N}-\text{NH}-\text{CO}-\text{A}-\text{CO}-\text{NH}-\text{NH}_2$$
wherein A is a substituted hydrocarbyl, unsubstituted hydrocarbyl, substituted heterocarbyl or unsubstituted heterocarbyl moiety, said moiety having one to twenty carbons or heteroatoms.
3. The microsphere of claim 2, wherein A is a heterocarbyl having heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur.
4. The microsphere of claim 2, wherein the carboxyl groups of the glucuronic acid residues have been activated with a carbodiimide.
5. The microsphere of claim 4, wherein the carbodiimide is 1-ethyl-dimethylaminopropyl carbodiimide.
6. The microsphere of claim 1, wherein the microsphere is formed by mixing hyaluronan and a dihydrazide in an aqueous solution, adding a substantially non-water miscible liquid and an emulsifying agent to form a water in oil type-emulsion, and lowering the pH of the emulsion.
7. The microsphere of claim 1, further comprising a component that is incorporated into the microsphere.

1 8. A method of making a functionalized hyaluronic acid microsphere comprising mixing hyaluronic  
2 acid and a dihydrazide with a crosslinking activator in an aqueous solution, adding a substantially  
3 non-water miscible liquid and an emulsifying agent to form an oil in water-type emulsion, and  
4 lowering the pH of the emulsion to allow intramolecular and intermolecular crosslinking to occur.

1 9. The method of claim 8, wherein the pH of the emulsion is lowered to the range from about pH 7  
2 to about pH 4.

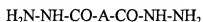
1 10. The method of claim 8, further comprising dehydrating the microspheres after they have formed.

1 11. The method of claim 8, wherein the crosslinking activator is a carbodiimide.

1 12. The method of claim 8, wherein at least one molar equivalent of a dihydrazide is added per molar  
2 equivalent of glucuronic acid groups on the hyaluronic acid.

1 13. The method of claim 8, wherein at least one molar equivalent of a carbodiimide is added per molar  
2 equivalent of glucuronic acid groups on the hyaluronic acid.

1 14. The method of claim 8, wherein the dihydrazide has the formula:



3 wherein A is a substituted hydrocarbyl, unsubstituted hydrocarbyl, substituted heterocarbyl or  
4 unsubstituted heterocarbyl moiety, said moiety having one to twenty carbons or heteroatoms.

1 15. The method of claim 8, wherein A is a substituted heterocarbyl or an unsubstituted heterocarbyl  
2 having heteroatoms selected from the group consisting of nitrogen, oxygen, or sulfur.

1 16. A pharmaceutical or cosmetic formulation comprising a pharmacologically effective amount of the  
2 microsphere of claim 7 and an acceptable carrier, excipient, or diluent.

- 1 17. A method of administering microspheres to a human or animal comprising administering a  
2 pharmacologically effective amount of the pharmaceutical or cosmetic formulation of claim 16.